DT-3073

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT:	Carsten Korth, et al.
SERIAL NO.	09/380,015
FILED:	August 23, 1999
FOR:	Immunological Detection of Prions
EXAMINER:	Ulrike Winkler, Ph.D Group: 1648

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION PURSUANT 37 CFR § 132

Sir:

1. I, Glenn Christopher Telling, presently residing at 1498 Leesburg Pike, Georgetown, Kentucky 40324, with a business address of 332 Health Sciences Research Building, University of Kentucky College of Medicine, Lexington, Kentucky 40536, declare as follows:

2. As listed in my *Curriculum Vitae*, I am presently an Associate Professor of Microbiology, Immunology and Molecular Genetics at the University of Kentucky, as well as an Associate Professor at the Department of Neurology of the University of Kentucky and in respect to the program in Gerontology of the University of Kentucky.

3. I have read and I am thoroughly familiar with the above-captioned patent application by Korth, et al., including the office actions of the United States Patent Office and the Interview Summary which was sent to the applicants on October 23, 2003.

4. I am also thoroughly familiar with U.S. Patent 5,846,533 to Pruisiner, et al. which was cited by the U.S. Examiner against the claims of the above-captioned Korth application. Moreover, I have read and am fully familiar with the Williamson, et al. publication, *Journal of Virology*, 1998 of which Dr. Pruisiner is a co-author and was submitted by the

applicant to demonstrate that the Pruisiner patent does not anticipate the invention of the above-captioned application and that Williamson and Pruisiner, in fact are at odds with each other.

5. Generally, since my study days at the University of Oxford, England, both for undergraduate and graduate degrees, I have worked in the field of molecular biology of infectious diseases . Since 1991, I have worked and done research in the field of prion technology when I joined the Pruisiner Group, initially as a post-doctoral fellow. Today, I am recognized as being well-versed in said technology.

6. My *Curriculum Vitae* is attached to this declaration. It will be noted that I have extensively published and lectured in the prion field and I am co-inventor of a number of U.S. and foreign patents, together with Dr. Pruisiner (See Section V(C) of the Curriculum Vitae. I therefore believe that I am qualified to render a reasoned opinion on the issues which have been raised by the United States Patent Office against the above-captioned application.

7. I have no financial or ownership interest in the above-captioned application or any patent that may be issued thereon.

8. PrP^{Sc} is a specific marker for prion diseases and is commonly thought to represent an integral part or even the entire infectious agent causing prion diseases like BSE in cattle or CJD in humans. PrP^{Sc} differs from the normal prion protein, PrP^{C}, in its three dimensional structure. There are, however, no differences in terms of amino acid-sequence or chemical modifications, i.e. the two proteins are identical after denaturation. Due to its different structure, PrP^{Sc} displays a higher resistance than PrP^{C} to enzymatic proteolysis, for example by proteinase K, (PK). PK treatment of PrP^{Sc} results in the persistence of a core molecule, referred to as PrP27-30.

9. Antisera to prion protein generally bind well to denatured PrP^{C} or PrP^{Sc} and to native PrP^{C}, but only weakly to native PrP^{Sc}. In the absence of a specific PrP^{Sc} binding antibody that would not cross-react with PrP^{C}, the presence of PrP^{Sc} has to be made evident in a two-step procedure using additional discriminatory criteria like protease resistance. In this case, PrP^{C} is first destroyed in a proteolytic reaction (commonly using PK), then PrP^{Sc} is detected using anti-PrP antibodies.

10. Obviously, an antibody detecting PrP^{Sc} without cross-reacting with PrP^{C} represents an invaluable tool both for research and diagnostic purposes, but despite years of intense efforts in the prion field it took until 1997 until this task was finally accomplished by Korth and co-workers (Nature 390, p74-77). In fact, up to this point in time it was not at all clear whether or not it would be theoretically possible that an antibody could bind to PrP^{Sc} without cross-reacting to PrP^{C}.

11. Consequently, up to 1997, immunological evidence for the presence of PrP^{Sc} described in the literature depended on additional steps required to discriminate between PrP^{Sc} and PrP^{C}, such as the above mentioned proteolytic removal of PrP^{C} from the sample. The patent document US5846533 of Prusiner et al., as well as other publications of Prusiner and colleagues (see below), is no different in this respect: All results presented in this document are based on immunologically detecting PrP^{Sc} after proteolytic removal of PrP^{C} by PK. Specifically:

- Figure 8 shows identification of PrP^{Sc} on histoblots which had been pre-treated with proteinase K to remove PrP^{C}
- Figures 9, 10, 11 and 12 show the reactivity of antibodies to native and denatured PrP27-30 either coated to ELISA plates (Fig 9 and 10) or in solution (Fig 11 and 12)

12. The evident conclusion for any person skilled in the art reading the Prusiner patent document is that the antibodies used cross-react with PrP^{C}: An experimenter

skilled in the art would not exercise the extra procedure of proteolytic removal of PrP^C prior to using an antibody that would not crossreact with PrP^C.

13. The invention described in the Prusiner Patent US5846533 is also discussed in further publications of Prusiner and colleagues:

14. The publication of Williamson et al., (J. Virol. 1998 p.9413-9418) describes the properties of a wide range of antibodies produced according to Patent US5846533. All antibodies tested showed strong binding to native PrP^C and to denatured PrP, one antibody also showed comparable binding to native PrP27-30. This means that the method in general led to conventional antibodies detecting PrP^C and denatured PrP and in some cases to antibodies capable of additionally binding to native PrP^{Sc}. However, the method did not produce antibodies binding only to PrP^{Sc} and not to PrP^C.

15. Antibodies R1, D14 and D18 described in the Williamson et al 1998 publication represent antibodies presented as examples of the invention in Patent US5846533. Reactivity to native PrP^{Sc} is claimed in Patent US5846533 for all three antibodies; however, in the aforementioned Williamson et al publication, only R1 binds to native PrP^{Sc} while neither D14 nor D18 show reactivity. All three antibodies exhibit strong reactivity to denatured PrP and native PrP^C, as demonstrated in Williamson et al 1998. Furthermore, it should be noted that specific panning methods of the phage clones did not enhance the properties of the resulting antibodies. Panning against PrP27-30 (D14, D18) resulted in even less favourable antibodies with questionable reactivity against native PrP^{Sc} compared to simply panning against recombinant PrP (R1).

16. From the above data, an experimenter skilled in the art has to conclude that the method described in Patent US5846533 leads to conventional antibodies binding to denatured PrP and native PrP^{C}, and in some cases to antibodies binding to denatured PrP, native PrP^{C} and native PrP^{Sc}, but the method is not suitable for producing antibodies specifically binding to native PrP^{Sc} without binding to native PrP^{C}.

17. Further to the points made above it should be noted that none of the further publications from the laboratory of Dr. S. Prusiner shows antibodies with a binding property preferring native PrP^{Sc} over native PrP^{C}, and the diagnostic prion-test recently developed in the laboratory of Dr. Prusiner and marketed by the company InPro (founded by Dr. Prusiner), which has been approved by the European Union for use in cattle and small ruminants, is based on a technology using conventional antibodies recognizing denatured PrP and native PrP^{C}, but not PrP^{Sc} (See COMMISSION REGULATION (EC) No 1053/2003).

18. The above-mentioned Interview Summary (see § 3) points out that the Williamson reference as published in the Journal of Virology 1998, volume 72, number 11, pages 9413-9418, indicates that two of the six antibodies disclosed in the Prusiner patent reference 5,846,533, as being part of the Pruisiner invention (see column 38, lines 20-21) do not immuno precipitate PrP 27-30 but only precipitate denatured PrP 2730. In view of this apparent discrepancy between the patent and the publication, the Interview Summary suggests that applicant provide evidence of the nature cited in point 1 and 2 of the Interview Summary as stated on page 2 of the Summary.

19. In view of my above explanation and opinion, it is obvious that following the procedure set out in the Pruisiner, et al. patent, a person skilled in the art would not believe that it would be likely that one could make antibodies – such as those disclosed and claimed in

the Korth, et al. application – that only react with the disease specific form of the prion protein without the use of the proteinase K and that the antibodies do not cross react with the normal cellular prior protein. I therefore believe that the point has been made above by me that the process of the Pruisiner patent cannot produce an antibody that is within the scope, or as the Summary states: „would infringe" the Korth application claims.

20. Moreover, it is also apparent from my above-explanations and opinion that using the two-step process of Pruisiner which includes a protease digestion step to detect the disease specific form of the prion protein implies clearly that the antibody failed to discriminate the infectious form from the cellular form.

21. Further, declarant sayeth not.

22. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statement and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: Dember 11th, 2003

Respectfully submitted.

Glenn Christopher Telling

Glenn Christopher Telling

CURRICULUM VITAE

Glenn Christopher Telling, M.A., Ph.D.
Ass ciate Professor

I. Biographical Information

A. Personal

Home Address:	1498 Leesburg Pike Georgetown, KY 40324
Home Phone:	(502) 570-9574
Business Address:	332 Health Sciences Research Building University of Kentucky College of Medicine Lexington, KY 40536
Business Phone:	(859) 323-8564 Office (859) 323-9819 Lab
Business Fax:	(859) 257-6151
Email:	gtell2@uky.edu

Birth Date:	October 2, 1957
Birthplace:	Cardiff, Wales
Citizenship:	American
Spouse:	Elizabeth Telling
Children:	Thazin (d.o.b. 05/23/86) Christopher (07/29/88) Maxine (10/14/02) Stella (10/14/02)

B. Education and Research Training

Undergraduate: Corpus Christi College, University of Oxford
B.A., Biochemistry, 1980

Graduate:

University of Oxford
M.A., Biochemistry, 1983

Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA
Summer Research Fellow: Insertion mutagenesis of the vacuolar protease *PRPB* gene of Saccharomyces cerevisiae using the γδ transposon. Advisor - Elizabeth Jones, Ph.D.

Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA
Ph.D. Biological Sciences - Doctoral Thesis: 'Genetic analysis of the functions of the adenovirus E1 proteins in oncogenic transformation and lytic infection'. Advisor – James F. Williams, Ph.D.

Postgraduate: Department of Biological Sciences, Carnegie Mellon University, Pittsburgh, PA

1990-1991Postdoctoral Fellow. Advisor - James F.Williams, Ph.D.

Department of Neurology, University of California, San Francisco
1991-1994 Postdoctoral Fellow. Advisor - Stanley B. Prusiner, M.D.

C. Academic App intments and P siti ns

1984-1985	Department of Biological Sciences Carnegie Mellon University Pittsburgh, PA	Teaching Assistant
1994-1996	Department of Neurology University of California San Francisco	Assistant Research Molecular Biologist
1996-1997	Department of Neurology University of California San Francisco	Assistant Professor
1997-1999	Medical Research Council Prion Unit Imperial College School of Medicine St. Mary's Hospital London	Senior Scientist and Program Leader
1999-2001	Department of Microbiology and Immunology University of Kentucky	Assistant Professor (Primary Appointment)
	Program in Gerontology University of Kentucky	Assistant Professor
2000-2001	Department of Neurology University of Kentucky	Assistant Professor
1998- 2003	Department of Pathology Colorado State University	Faculty Affiliate

Current positions

2001-present	Department of Microbiology, Immunology and Molecular Genetics University of Kentucky	Associate Professor (with tenure)
	Department of Neurology University of Kentucky	Associate Professor
	Program in Gerontology University of Kentucky	Associate Professor
2002 – present	Sanders-Brown Center on Aging College of Medicine University of Kentucky	Associate Professor

D. Honors and Awards

1991-1994	NIH Postdoctoral Fellowship
1996 –1997	Alexander von Humboldt-Stiftung, German American Academic Council Foundation Research Award in Support of Young Scientists and Scholars from the United States and Germany
1999	University of Kentucky Research Challenge Trust Fund Faculty (RCTF) Appointee
2004	Selected faculty participant in the University of Kentucky – Shandong University (China) faculty exchange program

E. Pr fessional Societies

American Society for Microbiology
American Society for Cell Biology
American Association for the Advancement of Science
Federation of American Societies for Experimental Biology

II. PROFESSIONAL ACTIVITIES

A. Review Activity, Funding Agencies (National and International)

2003	Reviewer for the ZNS1 SRB-W (01) Fogarty Adults Special Emphasis Panel "Brain Disorders in the Developing World: Research across the Lifespan", National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health (NIH)
2001- present	Member of the National Institutes of Health (NIH) Brain Disorders and Clinical Neuroscience's Study Section-3 (BDCN-3)
2002	Member of the United States Army Medical Research and Development Command, Program in Prion Research Study Section
2002	Member of Site Visiting Committee to review Dr. Stanley Prusiner's NIH National Institutes on Aging (NIA) Program Project Grant, 'Novel therapeutics for prion diseases', University of California, San Francisco
2002	Member of the Site Visiting Committee to review future Biological Sciences Research Council (BBSRC) -sponsored TSE research at the Institute for Animal Health, UK
2001	Chair, Sub-committee to review Transmissible Spongiform Encephalopathies Programs: Biological Sciences Research Council (BBSRC) 2001 Institute Assessment Exercise
2001	Member of the Site Visiting Committee to review research at the Institute for Animal Health, UK, for allocation of the 2002-2006 Competitive Strategic Grant for the UK Biotechnology and Biological Sciences Research Council (BBSRC) 2001 Institute Assessment Exercise
2000	Member of the scientific advisory panel for the UK Ministry of Agriculture Food and Fisheries (MAFF) Transmissible Spongiform Encephalopathies (TSE) research and surveillance program
1998-1999	Member of the UK Biotechnology and Biological Sciences Research Council (BBSRC) biology of spongiform encephalopathies program (BSEP) research funding advisory panel
1994-present	*Ad hoc* referee for the following funding agencies (on average 3 to 4 grants reviewed per year):

US Alzheimer's disease and Related Disorders
National Institutes of Health (NIH)
National Science Foundation (NSF)
UK Medical Research Council (MRC)

Comitato Promotore Telethon (Italy) research grants
Special Trustees for St Thomas' Hospital Research Endowments Committee
UK Biotechnology and Biological Sciences Research Council (BBSRC)
UK Ministry of Agriculture Food and Fisheries (MAFF)
Indiana Alzheimer Disease Center
UK Department of Health

B. Membership of other scientific committees, advisory panels and consultancies

2002	Member of the committee to develop an NIH-Sponsored TSE Reagent Repository Workshop
2002- present	Scientific consultant to Millennium Pharmaceuticals Inc., Cambridge, MA
2002- present	Member of the CWD advisory panel, Kentucky Department of Fish and Wildlife Resources
2001- present	Scientific consultant to Chiron, Inc., Emeryville CA
2001- present	Member of the scientific advisory panel for the US Creutzfeldt-Jakob Disease Foundation
2000- present	Member of the External Advisory Committee for the Indiana Alzheimer Disease Center
2000	Scientific consultant to the law firms of Thomas J. Amidon, Stowe, Vermont and Pierson, Wadham, Quinn and Yates, Burlington, Vermont
1999-2000	Member of the steering committee for the UK Biotechnology and Biological Sciences Research Council (BBSRC), Ministry of Agriculture Food and Fisheries (MAFF), Medical Research Council (MRC) and Department of Health sponsored Transmissible Spongiform Encephalopathies (TSE) workshop, April 2000
1998	Scientific consultant to the law firm of Burditt and Radzius, San Francisco, California: Risks of infectivity of a TSE/BSE agent associated with proteins isolated from the milk of transgenic animals
1996	*Ad Hoc* committee member to provide information bearing on the risk of the transmission of Creutzfeldt-Jakob disease from the administration of blood, blood components, or blood derivatives: Federal Drug Administration (FDA) and the National Heart, Lung and Blood Institute (NHLBI)
1996-1999	Member of the organizing committee for the 3rd, 4th and 5th Annual German-American Frontiers of Science Symposium: National Academy of Sciences (NAS), the Max-Planck-Society and the German American Academic Council (GAAC)

C. Review Activity, Journals

On average, 5 to 6 manuscripts reviewed per year

Science
Nature
Nature Medicine
EMBO Journal
Journal of General Virology
Neurology
Molecular Reproduction
Brain Research
Journal of the Royal College of Physicians of London
Journal of Clinical Pathology
Journal of Neurochemistry
Royal Society Proceedings: Biological Sciences

Neuroscience Letters
Molecular Medicine Today
American Journal of Pathology
Trends in Neurosciences
Lancet
Biochemistry
Trends in Cell Biology
Proceedings of the National Academy of Sciences (PNAS)
Trends in Microbiology
Journal of Biological Chemistry
Neuropathology and Applied Neurobiology

III. EDUCATIONAL ACTIVITIES

A. C urses Taught

1997	Visiting lecturer, University of California, Berkeley	
1997	Visiting lecturer, University Pacific School of Dentistry, San Francisco	
1996 – 1997	Organizing teaching seminars for a group that included 20 postdoctoral fellows , Department of Neurology, University of California, San Francisco	
1998	Lecturer, B.Sc. Clinical Sciences and M.Sc. Molecular Genetics, Imperial College School of Medicine, St. Mary's Hospital, London	

University of Kentucky

2004	Instructor, MI615: Molecular Biology	
2004	Instructor, MI 710-002: Molecular Virology	
2000 - 2003	GRN650, Research Methods in Gerontology (Course Director)	125 Contact hours
2000 - present	Instructor, MI822: Infection, Immunity and Disease	25 Contact hours
	Lectures Viral Genetics Prions and Diseases Dicussion Groups DC#3 – Childhood Viral Diseases DC#5 – Vector-borne viruses	
1999	GRN650, Research Methods in Gerontology, Transgenic methods in aging research	
2001	PGY618, Molecular Neurobiology, Prions and Prion Diseases	
2000 - present	MI772, Seminar in Microbiology	34 Contact hours
2002	Organizer of the Cellular and Molecular Mechanisms of Neurodegenerative Diseases Journal Club	

Mentored MI772 Students (Seminar in Microbiology)

2000	Nadia El-Guendy

B. Mentored Research Fell ws and Research Associates

1996 – 1997	Norbert Heye, M.D. – University of California, San Francisco
1996 – 1997	Dong Han, M.D. – University of California, San Francisco
1997 – 1999	Ulla Dennehy - MRC Prion Unit London
1997 – 1999	Susan Campbell - MRC Prion Unit London
2001	Anthony Ashworth, PhD – University of Kentucky
2002 – present	Yadavalli Rajgopal, PhD – University of Kentucky
2002 – present	Bian Jifeng M.D., Ph.D, Visiting Scientist -Associate Professor, Laboratory of Molecular Biology, Shandong University School of Medicine
1999 – 2001	Aisling Power, MSc
2001 – 2003	Adrian Centers, MS

C. Mentored Graduate Students

Adrian Centers - Rotation Project Advisor, Department of Microbiology and Immunology (1999 – 2000); PhD thesis research project Advisor (2000 – 2001)

Shawn Browning - Rotation Project Advisor, Department of Microbiology and Immunology (1999 – 2000); PhD thesis research project Advisor (2000 – present)

Sarah Goes - Rotation Project Advisor, Department of Microbiology and Immunology (2000 – 2001)

Melissa Hines - Rotation Project Advisor, Department of Microbiology and Immunology (2001)

Michael Jernigan - Rotation Project Advisor, Department of Microbiology and Immunology (2001); PhD thesis research project Advisor (2001 – present)

Karah Nazor - Rotation Project Advisor, Program in Gerontology (2000 – 2001); PhD thesis research project Advisor (2001 – present)

Maile Brown- Rotation Project Advisor, Program in Gerontology (2000 – 2001)

John Carmen - Rotation Project Advisor, Integrated Biomedical Sciences (2002)

Bei Dong - Rotation Project Advisor, Integrated Biomedical Sciences (2003); PhD thesis research project Advisor (2003 – present)

Matthew Garcia - Rotation Project Advisor, Integrated Biomedical Sciences (2003)

Christina Sigurdson, College of Veterinary Medicine and Biomedical Sciences, Department of Pathology, Colorado State University – Doctoral Thesis Adviser and External Examiner (1997-2001)

Charles A. Wuertzer, University of Rochester, Center for Aging and Developmental Biology, Division of Gene Therapy and Molecular Medicine - Doctoral Thesis Adviser (2002- present)

Barry Robinson, College of Medicine, Department of Microbiology, Immunology and Molecular Genetics University of

Kentucky - Doctoral Thesis Adviser (2002- present)

Josh Hood, College of Medicine, Department of Microbiology, Immunology and Molecular Genetics, University of Kentucky - Doctoral Thesis Adviser (2002- present)

Jill Gee, College of Medicine, Department of Anatomy and Neurobiology, University of Kentucky - Doctoral Thesis Adviser (2002- present)

D. Mentored Undergraduate Students

Leigh Wilson, University of Kentucky - "Bucks for Brains" research student advisor (2003)

IV. UNIVERSITY SERVICE

University of Kentucky

2003 – present	University Research Advisory Committee
2002	Chair, Search Committee for Chair of the Department of Physiology
2002	Member, Planning Committee to establish a Regional Center of Excellence in Emerging Diseases at the University of Kentucky
2002-2005	Member of the Institutional Biosafety Committee
2001- present	Member, Steering Committee, Graduate Program in Gerontology
2000 – 2001	Member, Recruitment Committee, Graduate Program in Gerontology
2001- present	Chair, Recruitment Committee, Graduate Program in Gerontology
2000	Chair, *ad hoc* committee to review research proposals for the Spinal Cord and Brain Injury Research Center, College of Medicine

Imperial College School of Medicine, London

1997-1999	Division of Neuroscience representative, Computer Users Consultative Committee

University of California, San Francisco

1994-1996	Co-ordination of scientific aspects of Licensing and Research Agreement: "Abbreviated Assays for Human and Domestic Animal Prions" between Centeon Inc. and U.C.S.F
1994-1997	Producing Patent Applications in liaison with patent lawyers and the University of California Office of Technology Transfer
1994-1997	Co-ordination of scientific and budgetary aspects of extra-mural grants and non-competitive grant renewals
1996-1997	Co-ordination of Annual Progress Reports for Centeon Inc./U.C.S.F. Research Agreement on Development of Improved Assay Systems for Detection of Human and Animal Prions
1997	Planning Committee for Annual Review of Sherman Fairchild Program in Neurodegenerative Diseases

V. RESEARCH ACTIVITIES

A. Active Support

Grant number:	N01-AI-25491
Role in Project :	Principal Investigator (30% effort)
Title:	US Based Collaboration in Emerging Viral and Prion Diseases
Awarding body:	NIH
Award period:	2002 - 2009
Funding Level:	$2,634,349

Grant number:	3 R01 NS40334-02S1
Role in Project:	Principal Investigator
Title:	Transgenetic studies of prion disease in cervids (Supplement)
Awarding body:	NIH
Award period:	2001 – 2003
Funding Level:	$750, 000

Grant number:	RO1 NS/AI40334-01
Role in Project:	Principal Investigator (30% effort)
Title:	Transgenetic studies of prion disease in cervids
Awarding body:	NIH
Award period:	2000 – 2003
Funding Level:	$869, 167

Role in Project:	Principal Investigator (0% effort)
Title:	Agreement with Institute of Animal Health to make transgenic mice
Awarding body:	Institute of Animal Health
Award period:	2002 – 2004
Funding Level:	$120,834

Role in Project:	Principal Investigator (0% effort)
Title:	Agreement with Chiron Corporation
Awarding body:	Chiron Inc.
Award period:	2003
Funding Level:	$8,214

Role in Project:	Co-Investigator (5% effort)
Title:	Genetic susceptibility and biological characterization of chronic wasting disease
Awarding body:	Department of Defense
Award period:	2002 – 2007
Funding Level:	$743,282 (Subcontract)

Grant number:	T32 AI49795
Title:	Training Program in Microbial Pathogenesis
Role in Project:	Training Faculty Member (for Shawn Browning)
Awarding body:	NIH
Award period:	2001 – 2006
Funding Level:	$18, 156/year

Title:	Molecular and Cellular Aspects of Brain Aging
Role in Project:	Training Faculty Member (for Michael Jernigan)
Awarding body:	NIH
Award period:	2002 – 2004
Funding Level:	$19, 656/year

B. Previous Support

Grant number:	P00034
Title:	*In vitro* studies of human prions
Role in Project:	Principal Investigator (10% effort)
Awarding body:	Pfizer/American Federation for Aging Research (AFAR) Research Grant in Age-Related Neurodegenerative Diseases
Award period:	2000 – 2001
Funding Level:	$50, 000
Awarding body:	NIH Academic Leadership Award and the Office of the Vice Chancellor for Research and Graduate Studies for the University of Kentucky Medical Center
Role in Project:	Principal Investigator (10% effort)
Award period:	1999 – 2000
Funding Level:	$15, 000
Awarding body:	UK Medical Research Council (MRC)
Role in Project:	Principal Investigator (100% effort)
Award period:	1997 – 2002
Funding Level:	£420, 000

C. Publications

US and International Patents

1. Prusiner, Stanley B; Glenn C. Telling; Fred E Cohen; Michael R. Scott: "Recombinant Construct Encoding Epitope Tagged PrP Protein" United States Patent Number 6,602,672. Issued August 5, 2003

2. Prusiner, Stanley B; Glenn C. Telling; Fred E Cohen; Michael R. Scott: "Transgenic animals expressing artificial epitope-tagged proteins" United States Patent Number 6,150,583. Issued November 21, 2000

3. Prusiner, Stanley B.; Michael R. Scott; Glenn C. Telling: "Detecting cow, sheep and human prions in a sample and transgenic mice used for same" United States Patent Number 6,008,435. Issued December 28, 1999.

   Associated International Patent: WO 9915640. Issued April 1, 1999

3. Prusiner, Stanley B.; Michael R. Scott; Glenn C. Telling: "Method of detecting prions in a sample and transgenic animal used for same" United States Patent Number 5,908,969. Issued June 1, 1999

4. Prusiner, Stanley B.; Michael R. Scott; Glenn C. Telling: "Detecting prions in a sample and prion preparation and transgenic animal used for same". United States Patent Number 5,792,901. Issued August 11, 1998.

   Associated International Patents: AU 6642796. Issued February 26, 1997
   WO 9704814. Issued February 13, 1997
   EP 0868201A. Issued October 7, 1998

5. Prusiner, Stanley B; Glenn C. Telling; Fred E Cohen; Michael R. Scott: "Transgenic animals expressing artificial epitope-tagged proteins" United States Patent Number 5,789,655. Issued August 4, 1998.

   Associated International Patents: EP 0915902A. Issued May 19, 1999
   WO 9746572. Issued December 11, 1997
   AU 3222197. Issued January 5, 1998

6. Prusiner, Stanley B.; Michael R. Scott; Glenn C. Telling: "Method of detecting prions in a sample and transgenic animal used for same" United States Patent Number 5,763,740. Issued June 9, 1998

7. Prusiner, Stanley B.; Michael R. Scott; Glenn C. Telling: "Method of detecting prions in a sample and transgenic animal used for same" United States Patent Number 5,565,186. Issued October 15, 1996.

Associated International Patents: AU 691277. Issued May 14, 1998
WO 9531466. Issued November 23, 1995

Papers submitted r in preparati n

1. Rajgopal Yadavalli, Rodney P. Guttmann, Tanya Seward, Adrian P. Centers, R. Anthony Williamson and Glenn C. Telling. Prion propagation is a calpain-dependent process. Submitted to Nature Medicine.

2. Moroncini, Gianluca, Nnennaya Kanu, Laura Solforosi, Erica Ollman Saphire, Glenn C. Telling, Jeremy Brockes, Dennis R. Burton and R. Anthony Williamson. Bespoke antibodies containing the replicative interface of cellular PrP are specific for PrP^{Sc}. Submitted to Nature Medicine.

3. Karah E. Nazor, Franziska Kuhn, Mike Green, Tanya Seward, Aisling M. Power, Alex Raeber and Glenn C. Telling. Immunodetection of PrP^{Sc} in a transgenic model of spontaneous prion disease using a scrapie-specific antibody. In preparation.

4. Michael Jernigan, Adrian Centers, Mike Green, Tanya Seward and Glenn C. Telling. Green fluorescent prion production in infected cell cultures and transgenic mice. In preparation.

5. Browning, Shawn, Tanya Seward, Mike Green, Christina Sigurson, Ed Hoover and Glenn Telling. Transmission of mouse-adapted scrapie and chronic wasting disease prions to transgenic mice expressing chimeric mouse-cervid and cervid PrP. In preparation

Papers published or in press

6. Korth, C., Kiyotoshi Kaneko, Darlene Groth, Norbert Heye, Glenn Telling, James Mastrianni, Piero Parchi, Pierluigi Gambetti, Robert Will, James Ironside, Cornelia Heinrich, Patrick Tremblay, Stephen J. DeArmond and Stanley B.Prusiner. Abbreviated incubation times for human prions in mice expressing a novel chimeric prion protein transgene. *Proc. Natl. Acad. Sci. USA*, 100 (8): 4784-4789, 2003

7. John G. Connolly, Roth J. Tate, Glenn C. Telling, Jan Fraser, Debbie Brown and Mark W. Head. Properties of the cellular prion protein expressed in *Xenopus* oocytes. *Neuroreport*, 13 (9): 1229-1233, 2002

8. Patrick J. Bosque, Chongsuk Ryou, Glenn Telling, David Peretz, Giuseppe Legname, Stephen J. DeArmond and Stanley B. Prusiner. Prions in skeletal muscle. *Proc. Natl. Acad. Sci. USA*, 99: 3812-3817, 2002

9. J. A. Mastrianni, S. Capellari, G. C. Telling, D. Han, P. Bosque, S. B. Prusiner, and S. J. DeArmond. Inherited prion disease caused by the V210I mutation: Transmission to transgenic mice. *Neurology*, 57: 2198-2205, 2001.

10. Telling, Glenn C. Protein-based PCR for prion diseases? *Nature Medicine*, 7(6): 11-12, 2001

11. Telling, Glenn C. Transgenic studies of prion diseases. *Methods in Molecular Medicine*, 58: 111-128, 2001

12. Campbell, Susan, Ulla Dennehy and Glenn Telling. Analyzing the influence of PrP primary structure on prion pathogenesis in transgenic mice. *Archives of Virology[Suppl]*, 16 : 87-94, 2000

13. Telling, G.C., Prion protein genes and prion diseases: studies in transgenic mice. *Neuropath. Appl. Neurobiol*, 26 209-220, 2000

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B ok Chapters

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Abstracts

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diseases in transgenic mice. 13th International Conference on Lymphoid Tissues in Immune Reactions, Geneva, Switzerland, August 1999

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74. Prusiner, Stanley B., Martin Vey and Glenn C. Telling: Prion formation and Chaperones. 10th International Congress of Virology, Jerusalem, Israel, 1996

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transgenes. *Neurology [Suppl.]*, 46 : 488, 1996

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81. Prusiner, S. B., K. -M. Pan, M. A. Baldwin, G. C. Telling and M. Scott: The prion diseases. *AIDS Res. Hum. Retroviruses [Suppl. 1]*, 11: S71, 1995

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86. Prusiner, S. B., G. Telling, D. Groth, M. Scott and S. J. DeArmond. Transgenetics of prion diseases. International Symposium on: "Where genotype does not match phenotype", Volterra, Italy, 1994

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89. Telling, G. C. and S. B. Prusiner. Altered patterns of expression of mutant forms of human PrP in neuroblastoma cells. Ninth International Congress of Virology, Glasgow UK, 1993

90. Telling, G., C. Liu and J. Williams. Constructing chimeric E1A genes and using them to locate an oncogenic determinant of type 12 adenovirus. Imperial Cancer Research Fund DNA Tumour Virus Symposium, Cambridge UK, 1993

91. Telling, G. C., S. Periera and J. Williams. A dubious oncogene; evidence that the product of the type 5 adenovirus E1B 19K gene is not required for transformation of rodent cells. Imperial Cancer Research Fund DNA Tumour Virus Symposium, Cambridge UK, 199

92. Hayes, B. W., G. C. Telling, J. F. Williams and S. J. Flint. An adenovirus 5 late non-structural protein regulates the efficiency of viral late mRNA translation. Cold Spring Harbor Laboratory Translational Control Symposium, Cold Spring Harbor Laboratory NY, 1990

Books

Molecular Mechanisms of Prion Diseases. Glenn C. Telling (Ed.) Horizon Scientific Press, UK (In Press)

D. Invited symposia and worksh ps

International Prion Conference: From Basic Research to Intervention Concepts, München – Germany, October 2003

"Prion propagtion is a calpain-dependent process"

Food Research Institute Annual Meeting, Madison WI, May 2003
"An Update on Chronic Wasting disease and other Prion diseases"

Chronic Wasting Disease Symposium, Denver, CO, August 2002
"Prion Diseases – Overview of General Concepts"
"Production and Preliminary Characterization of Transgenic Mice for studying Chronic Wasting Disease"

NIH-sponsored TSE workshop, Bethesda, MD, February 2002

7th Conference on Neurodegenerative Disorders: Common Molecular Mechanisms. Montego Bay, Jamaica, April, 2002

Interdisciplinary Conference on State Law and Public Health, Lexington, KY, October 2001
"Policy Issues in Bovine Spongiform Encephalopathy and other food borne diseases"

Chronic Wasting Disease Symposium, Kansas Department of Wildlife and Parks, Wichita, KS, September 2000
"Transgenic mice for studying Chronic Wasting Disease"

Symposium on the neuropathology of neurodegenerative diseases, Indiana University, June 2001
"New transgenic and *in vitro* approaches for studying prion diseases"

First Conference of the Creutzfeldt-Jakob Disease Foundation, Inc., Miami, Florida, May 2000
"Studying human prion diseases in transgenic mice"

Biotechnology and Biological Sciences Research Council (BBSRC) Biology of Spongiform Encephalopathies (BSEP) Workshop, Keele, UK, April 2000 (*Organizer and Chair*)
"Perspectives on the use of transgenic mice"

International Symposium on the characterization and diagnosis of prion diseases in animals and man, Tubingen, Germany, September 1999 (*Chair*)
"Transgenic studies of prion transmission barriers"

13th International Conference on Lymphoid Tissues in Immune Reactions, Geneva, Switzerland, August 1999
"Prion strains and species barriers: Investigating Creutzfeldt Jakob disease, BSE and other prion diseases in transgenic mice"

XVIII Summer Course at Universidad del Pais Vasco/Euskal Herriko Unibersitatea, San Sebastian, Spain, July 1999
"Bovine Spongiform Encephalopathy in the United Kingdom and the relationship with the new variant of Creutzfeldt-Jakob Disease in humans: An Update"

National Academy of Sciences (NAS) and the German American Academic Council's 5th Annual German-American Frontiers of Science Symposium: Potsdam, Germany, June 1999 (*Organizer*)

Critical data and scientific uncertainties: The statistics of transmissible spongiform encephalopathies (TSE's), Isaac Newton Institute for Mathematical Sciences, University of Cambridge, November 1998

National Academy of Sciences (NAS) and the German American Academic Council's 4th Annual German-American Frontiers of Science Symposium, Irvine. California, June 1998 (*Organizer*)

Institute of Psychiatry Short Course in Old Age Psychiatry, Institute of Psychiatry, Kings College London, September 1998
"Transmissible Dementias"

6th International Conference on Alzheimer's Disease and Related Disorders, Amsterdam, The Netherlands, July 1998

"Transgenic Mouse Models of Prion Diseases"

'Successfully Managing the TSE Crisis', Second IIR Ltd. Sponsored Symposium, London, June 1998
"Insights into the mechanisms of prion propagation from transgenic mouse studies"

Biomed 2 - Third Collaborators' Meeting, St Moritz, Switzerland, March 1998.
"Strains, species barriers and mechanisms of prion propagation: studies with transgenic mice"

Biotechnology and Biological Sciences Research Council (BBSRC) Biology of Spongiform Encephalopathies (BSEP) Workshop, University of Warwick, March 1998
"Prion strains and species barriers: studies with transgenic mice"

'Successfully Managing the TSE Crisis', IIR Ltd. Sponsored Symposium, London, March 1998
"Insights into the mechanisms of prion propagation from Transgenic mouse studies"

Royal College of Physicians, Advanced Medicine Conference, London, February 1998
"BSE"

Microsymposium on Prions and Prion Diseases, Institut Fur Molekularbiologie Abteilung I, Universitat Zurich, Switzerland, December 1997
"Prion strains and species barriers: an update on transgenic mouse work"

National Academy of Sciences' (NAS) 9th Annual Frontiers of Science Symposium, Irvine CA, November 1997
"Transgenic Models of Prion Diseases"

Joint Congress of the German Societies of Clinical Chemistry and Laboratory Medicine on Molecular Diagnostics, Munster Germany, September 1997
"Diagnostic markers of prion disease"

The Congress of the Institute of Biomedical Science, Biomedical Science Congress, International Convention Centre, Birmingham UK, September 1997
"BSE and the public health"

National Academy of Sciences (NAS), Max-Planck-Society and the German American Academic Council's 3rd Annual German-American Frontiers of Science Symposium, Munich, Germany, June 1997 (*Organizer*)

2nd Annual Centeon/ UCSF Meeting, Monterey CA, April 1997
"New Models and Validation of the Transgenic Human Prion Assay"-

International Symposium on Spongiform Encephalopathies: Generating Rational Policy in the Face of Public Fears. The Ceres Forum of the Center for Food and Nutrition Policy at Georgetown University and the American Association of the Vetinary Medical Colleges, Georgetown University, Washington DC, December 1996
"Prion Research"

National Academy of Sciences' (NAS) 8th Annual Frontiers of Science Symposium, Irvine CA, November 1996

National Academy of Sciences (NAS), German American Academic Council 2nd Annual Symposium on German-American Frontiers of Science, Woods Hole MA, June 1996
"Prion Propagation and Protein X using Transgenic Mice"

96th General Meeting of the American Society for Microbiology. Prion Proteins Session: "A Novel Mechanism for Inheritance", New Orleans LA, May 1996
"Prion Biology and Diseases of Mammals"

1st Annual Centeon/ UCSF Meeting, Napa Valley CA, April 1996
"Abbreviated Assays for Human and Domestic Animal Prions"

Food and Drug Administration (FDA) and the National Heart, Lung and Blood Institute (NHLBI), Bethesda MD, January 1996

"Optimal methods to detect prion infectivity in human blood: Transgenic mice expressing human and chimeric human-mouse prion proteins"

Symposium on the Molecular Biology of Prions and Pathology of Prion Diseases, The Banbury Center, Cold Spring Harbor Laboratory NY, November, 1995

"Prion propagation and protein X in transgenic mice"

6th International Workshop on Bovine Spongiform Encephalopathy, Williamsburgh VA, February 1995

"Transgenic mouse models of human prion diseases"

Serono Symposia International Symposium on: Where genotype does not match phenotype, Volterra, Italy, October 1994

"Transgenetics of prion diseases"

9th International Congress of Virology, Glasgow, UK, August 1993

"Altered patterns of expression of mutant forms of human PrP in neuroblastoma cells"

Imperial Cancer Research Fund DNA Tumor Virus Symposium, Cambridge UK, 1991

"A dubious oncogene; evidence that the product of the type 5 adenovirus E1B 19K gene is not required for transformation of rodent cells"

E. Invited lectures

Department of Molecular and Cellular Biochemistry, Ohio State University, January 2004

"Transgenic and cell culture approaches for studying the mechanism of prion propagation"

Department of Neurology Grand Rounds, University of Kentucky, January 2004

"Transgenic and cell culture approaches for studying the mechanism of prion propagation"

Department of Biochemistry and Medicine, Dartmouth Medical School, NH, April 2003

"Transgenic and cell culture models of human and animal prion diseases"

Department of Pathology and Laboratory Sciences, University of Ottawa, Canada, June 2002

"Transgenic and cell culture models of human and animal prion diseases"

Division of Infectious Diseases, University of Kentucky, Lexington, April 2002

"Prions"

Chiron, Inc. San Francisco, CA, November 2001

"Transgenic mice for studying prion diseases"

Nathan Shock Center on Aging Seminar Series, University of Rochester School of Medicine and Dentistry, New York, December 2001

"Transgenic and *in vitro* approaches for studying prion diseases"

Department of Pathology, University of Kentucky, Lexington, January 2001

"Prions"

Department of Biological Sciences, University of Kentucky, Lexington, November 2000

"Transgenic approaches for studying prion diseases"

Sanders-Brown Center on Aging Seminar Series, University of Kentucky, October 2000

"New transgenic and *in vitro* approaches for studying prion diseases"

Department of Molecular and Cell Biology, University of Texas, Dallas, September 2000

"Deciphering prion diseases using transgenic mice"

Department of Neurology, University of Kentucky, Lexington, February 2000

"Transgenic models of CJD"

Department of Pathology, Case Western Reserve University, February 2000
"Transgenic approaches for studying prion diseases"

Division of Medical and Molecular Genetics, King's College at Guy's Hospital, London, April 1999
"Deciphering prion diseases using transgenic mice"

Sanders-Brown Center on Aging, University of Kentucky, Lexington, April 1999
"Deciphering prion diseases using transgenic mice"

Department of Molecular, Cellular and Developmental Biology, University of Colorado, October 1998
"Deciphering prion diseases with transgenic mice"

Department of Pathology, Colorado State University, October 1998
"Deciphering prion diseases with transgenic mice"

Institute of Animal Technology, Institute of Psychiatry, Kings College London, May 1998
"Prion hypothesis"

Institute for Animal Health, Neuropathogenesis Unit, Edinburgh, April 1998
"Transgenetic investigations of TSE's"

Institute of Psychiatry, Department of Neuroscience, London, January 1998
"Transgenic Models of Prion Diseases"

Division of Biomedical Sciences, Imperial College of Medicine at St. Mary's, December 1997
"Transgenetic investigations of prion diseases"

University of Birmingham, September 1997
"Transgenetic investigations of prion diseases"

Max von Pettenkofer Institut, University of Munich, Munich, Germany, June 1997
"Investigating Prion Diseases with Transgenic Mice"

University Pacific School of Dentistry, San Francisco CA, May 1997
"Prion Proteins and Mad Cow Disease: Should a Dentist be Concerned?"

University of California, Berkeley, May 1997
"Prions"

Neurogenetics Unit, Imperial College of Medicine at St Mary's, January 1997
"Transgenic Mice and the Prion Diseases: Recent Breakthroughs and Future Directions"

Departments of Biological Sciences, Carnegie Mellon University and University of Pittsburgh, Pittsburgh PA, November 1995
"Prion transmission from humans to transgenic mice: Insights into the mechanisms of prion propagation"

Gene Therapy Center, University of North Carolina at Chapel Hill, Chapel Hill NC, June 1995
"Mechanisms of Prion Propagation from Transgenic mice expressing chimeric human-mouse prion proteins"

Miles (Bayer) Inc., Berkeley CA, March 1995
"Prion transmission from humans to mice: Evidence for a species-specific factor in disease propagation"

Department of Biochemistry and Biophysics, University of California, San Francisco CA, March 1995
"Transgenic mice for studying human prion diseases"

Medical Research Council (MRC), Laboratory of Molecular Biology, Cambridge, UK, June 1994

"Transgenic mice for studying human prion diseases"

The George Williams Hooper Foundation, University of California, San Francisco CA, December 1990
"Genetic analysis of the functions of the adenovirus E1 proteins in oncogenic transformation and lytic infection"